

Ifw



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Kevin J. Tracey  
Application No.: 10/535,267 Group Art Unit: 1642  
Filed: November 22, 2005 Examiner: Not Assigned  
Confirmation No.: 6690  
Title: USE OF HMGB POLYPEPTIDES FOR INCREASING IMMUNE RESPONSES

CERTIFICATE OF MAILING OR TRANSMISSION	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, or is being facsimile transmitted to the United States Patent and Trademark Office on:	
May 31, 2006	Christine A. Budd
Date	Signature
CHRISTINE A. BUDD	
Typed or printed name of person signing certificate	

INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This Information Disclosure Statement is submitted:

- ☐ under 37 CFR 1.129(a), or  
(First/Second submission after Final Rejection)
- ☒ under 37 CFR 1.97(b), or  
(Within any one of the following time periods: three months of filing national application (other than a CPA) or date of entry of the national stage in an international application; or before the mailing date of a first office action on the merits in a non-provisional application, including a CPA, or a Request for Continued Examination).
- ☐ under 37 CFR 1.97(c) together with either:
- ☐ a Statement under 37 CFR 1.97(e), as checked below, or
- ☐ a \$180.00 fee under 37 CFR 1.17(p), or  
(After the 37 CFR 1.97(b) time period, but before final action or notice of allowance, whichever occurs first)
- ☐ under 37 CFR 1.97(d) together with:
- ☐ a Statement under 37 CFR 1.97(e), as checked below, and
- ☐ a \$180.00 fee under 37 CFR 1.17(p), or  
(Filed after final action or notice of allowance, whichever occurs first, but on or before payment of the issue fee)
- ☐ under 37 CFR 1.97(i):  
Applicant requests that the IDS and cited reference(s) be placed in the application filewrapper.  
(Filed after payment of issue fee)



Statement Under 37 CFR 1.97(e)

- ☐ Each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement; or
- ☐ No item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

Statement Under 37 CFR 1.704(d) (Patent Term Adjustment)

Applies to original applications (other than design) filed on or after May 29, 2000

- ☐ Each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.
- ☒ Enclosed herewith is form PTO-1449:
  - ☒ Copies of the cited references, B1-B8 and C1-C80, are enclosed.
    - ☐ Since this application was filed after June 30, 2003, copies of issued U.S. patents and published U.S. applications are not required and are not being provided.
  - ☐ Copies of the cited references are enclosed except those entered in prior application, U.S. Application No. [ ], to which priority under 35 U.S.C. 120 is claimed. [The earlier application contains copies of the cited references.]
  - ☒ The listed references (A1, C1-C4) were cited in the enclosed International Search Report in a counterpart foreign application.
  - ☒ The "concise explanation" requirement (non-English references) for references B5 and B8 under 37 CFR 1.98(a)(3) is satisfied by:
    - ☐ the explanation provided on the attached sheet.
    - ☐ the explanation provided in the Specification.
    - ☐ submission of the enclosed International Search Report.
    - ☐ submission of the enclosed English-language version of a foreign Search Report and/or foreign Office Action.
    - ☒ the enclosed English language abstract.



- ☐ Applicant requests that the following non-published pending applications be considered:  
(Affix a label or apply the stamp "Non-Published IDS Reference - Do Not Scan" to the front of each unpublished pending appl'n.)

Examiner's  
Initials

\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]  
\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]  
\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_  
Examiner

\_\_\_\_\_  
Date

- ☐ A copy of each above-cited application, including the current claims, is enclosed, except any application filed on or after June 30, 2003, which has been scanned into the PTO's Image File Wrapper (IFW) system and is available to the examiner.
- ☐ A copy of each above-cited application, including the current claims, is enclosed, except those entered in prior application, U.S. Application No. [ ], to which priority under 35 U.S.C. 120 is claimed.

The Examiner is requested to return a copy of the above list of pending applications indicating which references were considered with the next office communication.

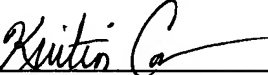
It is requested that the information disclosed herein be made of record in this application.

Method of payment:

- ☐ A check for the fee noted above is enclosed, or the fee has been included in the check with the accompanying Reply. A copy of this Statement is enclosed.
- ☐ Please charge Deposit Account 08-0380 in the amount of \$[ ]. A copy of this Statement is enclosed.
- ☒ Please charge any deficiency in fees and credit any overpayment to Deposit Account 08-0380.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By 

Kristin A. Connarn

Registration No.: 57,025

Telephone: (978) 341-0036

Facsimile: (978) 341-0136

Concord, MA 01742-9133

Dated: May 31, 2006

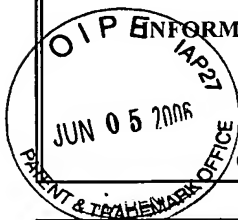


PTO-1449 REPRODUCED

ATTORNEY DOCKET NO.  
3268.1003-004APPLICATION NO.  
10/535,267FIRST NAMED INVENTOR  
Kevin J. TraceyFILING DATE  
November 22, 2005EXAMINER  
Not AssignedCONFIRMATION NO.  
6690GROUP  
1642INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION

May 31, 2006

(Use several sheets if necessary)



## U.S. PATENT DOCUMENTS

EXAM- INER INI- TIAL	REF. NO.	DOCUMENT NUMBER Number-Kind Code (if known)	ISSUE DATE / PUBLICATION DATE MM-DD-YYYY	NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT
	A1	6,649,172 B2	11/18/2003	Johnson, D.
	A2	6,303,321 B1	10/16/2001	Tracey, K. J. and Wang, H.
	A3	6,448,223 B1	09/10/2002	Tracey, K. J. and Wang, H.
	A4	6,468,533 B1	10/22/2002	Tracey, K. J. and Wang, H.
	A5	2003/0060410 A1	03/27/2003	Tracey, K. J., <i>et al.</i>
	A6	2003/0144201 A1	07/31/2003	Tracey, K. J., <i>et al.</i>
	A7	2004/0005316 A1	01/08/2004	Tracey, K. J., <i>et al.</i>
	A8	2004/0053841 A1	03/18/2004	Tracey, K. J., <i>et al.</i>
	A9	6,171,779 B1	01/09/2001	Chada, K.K., <i>et al.</i>
	A10	6,720,472 B2	04/13/2004	Chada, K.K., <i>et al.</i>
	A11	2002/0009749 A1	01/24/2002	Ozaki, S., <i>et al.</i>
	A12	6,323,329 B1	11/27/2001	Bullerdiel, J.
	A13	5,594,114	01/14/1997	Goodearl, A. D. J., <i>et al.</i>
	A14	2003/0017155 A1	01/23/2003	Tracey, K. J., <i>et al.</i>
	A15	2003/0143194 A1	07/31/2003	Tracey, K. J., <i>et al.</i>
	A16	2004/0120953 A1	06/24/2004	Tracey, K. J., <i>et al.</i>
	A17	5,545,806	08/13/1996	Lonberg, <i>et al.</i>
	A18	5,545,807	08/13/1996	Surani, A.M., <i>et al.</i>
	A19	5,605,690	02/25/1997	Jacobs, C.A., <i>et al.</i>
	A20	5,656,272	08/12/1997	Le, J., <i>et al.</i>
	A21	6,177,077 B1	01/23/2001	Tobnick, E.L.
	A22			
	A23			
	A24			
	A25			

EXAMINER

DATE CONSIDERED



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>May 31, 2006</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned		CONFIRMATION NO. 6690	GROUP 1642

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER Country Code-Number-Kind Code (if known)	DATE MM-DD-YYYY	NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT	TRANSLATION YES NO	
	B1	WO 00/47104	08/17/2000	The Picower Institute for Medical Research		
	B2	WO 99/59609	11/25/1999	Bartorelli, A.		
	B3	WO 02/074337 A1	09/26/2002	Bianchi, M. E., <i>et al.</i>		
	B4	WO 2004/004763 A2	01/15/2004	Bianchi, M. E., <i>et al.</i>		
	B5	JP 62-166897	07/23/1987	Toyo Soda Mfg. Co. Ltd.		X
	B6	EP 1 079 849 B1	01/02/2002	Bartorelli, A.		
	B7	WO 96/25493	08/22/1996	Bullerdiek, J.		
	B8	WO 97/23611	07/03/1997	Bullerdiek, J.		X
	B9					
	B10					
	B11					
	B12					
	B13					
	B14					
	B16					
	B16					
	B17					
	B18					
	B16					
	B23					
	B21					
	B22					
	B23					
	B24					

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  May 31, 2006  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned	CONFIRMATION NO. 6690	GROUP 1642	

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C1	Andersson, U., <i>et al.</i> , "High Mobility Group 1 Protein (HMG-1) Stimulates Proinflammatory Cytokine Synthesis in Human Monocytes," <i>J. Exp. Med.</i> , 192(4):565-570 (2000).
C2	Czura, C., <i>et al.</i> , "Dual Roles for HMGB1: DNA Binding and Cytokine," <i>J. Endotoxin Res.</i> , 7(4):315-321 (2001).
C3	Wen, L., <i>et al.</i> , "A Human Placental cDNA Clone that Encodes Nonhistone Chromosomal Protein HMG-1," <i>Nucleic Acids Res.</i> , 17(3):1197-1213 (1989).
C4	Lode, <i>et al.</i> , "Targeted Cytokines for Cancer Immunotherapy," <i>Immunologic Research</i> , 21(2-3):279-288 (2000).
C5	Abaza, M.-S. I. and Atassi, M. Z., "Effects of Amino Acid Substitutions Outside an Antigenic Site on Protein Binding to Monoclonal Antibodies of Predetermined Specificity Obtained by Peptide Immunization: Demonstration with Region 94-100 (Antigenic Site 3) of Myoglobin," <i>J. Protein Chem.</i> 11(5):433-444 (1992).
C6	Abraham, E., <i>et al.</i> , "Cutting Edge: HMG-1 as a Mediator of Acute Lung Inflammation," <i>J. Immunol.</i> , 165:2950-2954 (2000).
C7	Bianchi, M., <i>et al.</i> , "Suppression of Proinflammatory Cytokines in Monocytes by a Tetravalent Guanyldiazide," <i>J. Of Exp. Med.</i> , 183:927-936 (1996).
C8	Ayer, L. M., <i>et al.</i> , "Antibodies to HMG Proteins in Patients With Drug-Induced Autoimmunity," <i>Arthritis Rheum.</i> , 37(1):98-103 (1994).
C9	Banks, G. C., <i>et al.</i> , "The HMG-I(Y) A-T-hook Peptide Motif Confers DNA-binding Specificity to a Structured Chimeric Protein," <i>J. Biol. Chem.</i> , 274(23):16536-16544 (1999).
C10	Baxevas, A. D. and Landsman, D., "The HMG-1 Box Protein Family: Classification and Functional Relationships," <i>Nucleic Acids Res.</i> , 23(9):1604-1613 (1995).
C11	Bianchi, M. E., <i>et al.</i> , "The DNA Binding Site of HMG1 Protein is Composed of Two Similar Segments (HMG Boxes), Both of Which Have Counterparts in Other Eukaryotic Regulatory Proteins," <i>EMBO J.</i> , 11(3):1055-1063 (1992).

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  May 31, 2006  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned	CONFIRMATION NO. 6690	GROUP 1642	

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C12	Bianchi, M. E., <i>et al.</i> , "Specific Recognition of Cruciform DNA by Nuclear Protein HMG1," <i>Science</i> , 243:1056-1059 (1989).
C13	Bustin, M., "Revised Nomenclature for High Mobility Group (HMG) Chromosomal Proteins," <i>Trends Biochem. Sci.</i> , 26:152-153 (2001).
C14	Bustin, M., <i>et al.</i> , "Antigenic Determinants of High Mobility Group Chromosomal Proteins 1 and 2," <i>Biochem.</i> , 21:6773-6777 (1982).
C15	Bustin, M., <i>et al.</i> , "Immunological Relatedness of High Mobility Group Chromosomal Proteins from Calf Thymus," <i>J. Biol. Chem.</i> , 253(5):1694-1699 (1978).
C16	Chou, D. K. H., <i>et al.</i> , "Identity of Nuclear High-Mobility-Group Protein, HMG-1, and Sulfoglucuronyl Carbohydrate-Binding Protein, SBP-1, in Brain," <i>J. Neurochem.</i> , 77:120-131 (2001).
C14	Colman, P. M., "Effects of Amino Acid Sequence Changes on Antibody-Antigen Interactions," <i>Res. Immunol.</i> , 145(1):33-36 (1994).
C18	Clackson, T., <i>et al.</i> , "Making Antibody Fragments Using Phage Display Libraries," <i>Nature</i> , 352: 624-628 (1991).
C19	Daston, M. M. and Ratner, N., "Expression of P30, a Protein with Adhesive Properties in Schwann Cells and Neurons of the Developing and Regenerating Peripheral Nerve," <i>J. Cell Biol.</i> 112(6):1229-1239 (1991).
C20	Degryse, B., <i>et al.</i> , "The High Mobility Group (HMG) Boxes of the Nuclear Protein HMG1 Induce Chemotaxis and Cytoskeleton Reorganization in Rat Smooth Muscle Cells," <i>J. Cell Biol.</i> , 152(6):1197-1206 (2001).
C21	Falciola, L., <i>et al.</i> , "High Mobility Group 1 Protein is Not Stably Associated with the Chromosomes of Somatic Cells," <i>J. Cell. Biol.</i> , 137(1):19-26 (1997).
C22	Freeman, B. D., <i>et al.</i> , "The Role of Inflammation in Sepsis and Septic Shock: A Meta-Analysis of Both Clinical and Preclinical Trials of Anti-Inflammatory Therapies," in <i>Inflammation: Basic Principles and Clinical Correlates</i> (John I. Gallin and Ralph Snyderman eds., Lippincott, Williams & Wilkins, Philadelphia, 3 <sup>rd</sup> ed.), pp 965-975 (1999).

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>May 31, 2006</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned		CONFIRMATION NO. 6690	GROUP 1642

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C23	Imamura, T., <i>et al.</i> , "Interaction with p53 Enhances Binding of Cisplatin-Modified DNA by High Mobility Group 1 Protein," <i>J. Biol. Chem.</i> , 276(10):7534-7540 (2001).
C24	Ise, T., <i>et al.</i> , "Transcription Factor Y-Box Binding Protein 1 Binds Preferentially to Cisplatin-Modified DNA and Interacts With Proliferating Cell Nuclear Antigen," <i>Cancer Res.</i> , 59:342-346 (1999).
C25	Johns, E. W., <i>et al.</i> , "History, Definitions and Problems," in <i>The HMG Chromosomal Proteins</i> , (London: Academic Press), pp. 1-7 (1982).
C26	Jung, F., <i>et al.</i> , "Antibodies Against a Peptide Sequence Located in the Linker Region of the HMG-1/2 Box Domains in Sera From Patients With Juvenile Rheumatoid Arthritis," <i>Arthritis Rheum.</i> , 40(10):1803-1809 (1997).
C27	Landsman, D. and Bustin, M., "A Signature for the HMG-1 Box DNA-Binding Proteins," <i>BioEssays</i> , 15(8):539-546 (1993).
C28	Lederman, S., <i>et al.</i> , "A Single Amino Acid Substitution in a Common African Allele of the CD4 Molecule Ablates Binding of the Monoclonal Antibody OKT4," <i>Mol. Immunol.</i> , 28(11):1171-1181 (1991).
C29	Ma, W., <i>et al.</i> , "Detection of Anti-neutrophil Cytoplasmic Antibodies in MRL/Mp- <i>lpr/lpr</i> Mice and Analysis of Their Target Antigens," <i>Autoimmunity</i> , 32(4):281-291 (2000).
C30	Melloni, E., <i>et al.</i> , "Identity in Molecular Structure Between 'Differentiation Enhancing Factor' of Murine Erythroleukemia Cells and the 30 kD Heparin-Binding Protein of Developing Rat Brain," <i>Biochem. Biophys. Res. Commun.</i> , 210(1):82-89 (1995).
C31	Melloni, E., <i>et al.</i> , "Extracellular Release of the 'Differentiation Enhancing Factor', a HMG1 Protein Type, is an Early Step in Murine Erythroleukemia Cell Differentiation," <i>FEBS Lett.</i> , 368:466-470 (1995).
C32	Merenmies, J., <i>et al.</i> , "30-kDa Heparin-Binding Protein of Brain (Amphoterin) Involved in Neurite Outgrowth," <i>J. Biol. Chem.</i> , 266(25):16722-16729 (1991).

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  May 31, 2006  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned		CONFIRMATION NO. 6690	GROUP 1642

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C33	Milev, P., <i>et al.</i> , "High Affinity Binding and Overlapping Localization of Neurocan and Phosphacan/Protein-Tyrosine Phosphatase - $\zeta/\beta$ with Tenascin-R, Amphoterin, and the Heparin-Binding Growth-Associated Molecule," <i>J. Biol. Chem.</i> 273(12):6998-7005 (1998).
C34	Mohan, P. S., <i>et al.</i> , "Sulfoglycolipids Bind to Adhesive Protein Amphoterin (p30) in the Nervous System," <i>Biochem. Biophys. Res. Commun.</i> , 182(2):689-696 (1992).
C35	Parkkinen, J. and Rauvala, H., "Interactions of Plasminogen and Tissue Plasminogen Activator (t-PA) with Amphoterin," <i>J. Biol. Chem.</i> , 266(25):16730-16735 (1991).
C36	Parkkinen, J., <i>et al.</i> , "Amphoterin, the 30-kDa Protein in a Family of HMG1-type Polypeptides," <i>J. Biol. Chem.</i> , 268(26):19726-19738 (1993).
C37	Passalacqua, M., <i>et al.</i> , "Stimulated Astrocytes Release High-Mobility Group 1 Protein, an Inducer of Lan-5 Neuroblastoma Cell Differentiation," <i>Neuroscience</i> , 82(4):1021-1028 (1998).
C38	Rauvala, H. and Pihlaskari, R., "Isolation and Some Characteristics of an Adhesive Factor of Brain That Enhances Neurite Outgrowth in Central Neurons," <i>J. Biol. Chem.</i> , 262(34):16625-16635 (1987).
C39	Rauvala, H., <i>et al.</i> , "The Adhesive and Neurite-Promoting Molecule p30: Analysis of the Amino-Terminal Sequence and Production of Antipeptide Antibodies That Detect p30 at the Surface of Neuroblastoma Cells and of Brain Neurons," <i>J. Cell Biol.</i> , 107(6):2293-2305 (1988).
C40	Romani, M., <i>et al.</i> , "Serological Analysis of Species Specificity in the High Mobility Group Chromosomal Proteins," <i>J. Biol. Chem.</i> , 254(8):2918-2922 (1979).
C41	Salmivirta, M., <i>et al.</i> , "Neurite Growth-Promoting Protein (Amphoterin, p30) Binds Syndecan," <i>Exp. Cell Res.</i> , 200:444-451 (1992).
C42	Scaffidi, P., <i>et al.</i> , "Release of Chromatin Protein HMGB1 by Necrotic Cells Triggers Inflammation," <i>Nature</i> , 418:191-195 (2002).
C43	Sobajima, J., <i>et al.</i> , "Prevalence and Characterization of Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (P-ANCA) Directed Against HMG1 and HMG2 in Ulcerative Colitis (UC)," <i>Clin. Exp. Immunol.</i> , 111:402-407 (1998).

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  May 31, 2006  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned	CONFIRMATION NO. 6690	GROUP 1642	

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C44	Sobajima, J., <i>et al.</i> , "Anti-Neutrophil Cytoplasmic Antibodies (ANCA) in Ulcerative Colitis: Anti-Cathepsin G and a Novel Antibody Correlate With a Refractory Type," <i>Clin. Exp. Immunol.</i> , 105:120-124 (1996).
C45	Sobajima, J., <i>et al.</i> , "Novel Autoantigens of Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (P-ANCA) in Ulcerative Colitis: Non-Histone Chromosomal Proteins, HMG1 and HMG2," <i>Clin. Exp. Immunol.</i> , 107:135-140 (1997).
C46	Sobajima, J., <i>et al.</i> , "High Mobility Group (HMG) Non-Histone Chromosomal Proteins HMG1 and HMG2 are Significant Target Antigens of Perinuclear Anti-Neutrophil Cytoplasmic Antibodies in Autoimmune Hepatitis," <i>Gut</i> , 44:867-873 (1999).
C47	Sparatore, B. <i>et al.</i> , "Extracellular High-Mobility Group 1 Protein is Essential for Murine Erythroleukaemia Cell Differentiation," <i>Biochem. J.</i> , 320:253-256 (1996).
C48	Suda, T., <i>et al.</i> , "A Novel Activity of HMG Domains: Promotion of the Triple-Stranded Complex Formation Between DNA Containing (GGA/TCC) <sub>11</sub> and d(GGA) <sub>11</sub> Oligonucleotides," <i>Nucleic Acids Res.</i> , 24(23):4733-4740 (1996).
C49	Tsuneoka, M., <i>et al.</i> , "Monoclonal Antibody Against Non-Histone Chromosomal Protein High Mobility Group 1 Co-Migrates With High Mobility Group 1 Into the Nucleus," <i>J. Biol. Chem.</i> , 261(4):1829-1834 (1986).
C50	Uesugi, H., <i>et al.</i> , "Prevalence and Characterization of Novel pANCA, Antibodies to the High Mobility Group Non-Histone Chromosomal Proteins HMG1 and HMG2, in Systemic Rheumatic Diseases," <i>J. Rheumatol.</i> , 25(4):703-709 (1998).
C51	Vanderbilt, J. N. and Anderson, J. N., "Monoclonal Antibodies as Probes for the Complexity, Phylogeny, and Chromatin Distribution of High Mobility Group Chromosomal Proteins 1 and 2," <i>J. Biol. Chem.</i> , 260(16):9336-9345 (1985).
C52	Wang, H., <i>et al.</i> , "HMG-1 as a Late Mediator of Endotoxin Lethality in Mice," <i>Science</i> , 285:248-251 (1999).
C53	Wang, H., <i>et al.</i> , "Proinflammatory Cytokines (Tumor Necrosis Factor and Interleukin 1) Stimulate Release of High Mobility Group Protein-1 by Pituicytes," <i>Surgery</i> , 126(2):389-392(1999).

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  May 31, 2006  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned	CONFIRMATION NO. 6690	GROUP 1642	

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C54	Yamawaki, M., <i>et al.</i> , "Generation and Characterization of Anti-Sulfoglucuronosyl Paragloboside Monoclonal Antibody NGR50 and its Immunoreactivity with Peripheral Nerve," <i>J. Neurosci. Res.</i> , 44:586-593 (1996).
C55	Yamada, S., <i>et al.</i> , "High Mobility Group Protein 1 (HMGB1) Quantified by ELISA with a Monoclonal Antibody That Does Not Cross-React with HMGB2," <i>Clin. Chem.</i> , 49(9):1535-1537 (2003).
C56	Zhang, M and Tracey, K. J., "Tumor Necrosis Factor," in <i>The Cytokine Handbook</i> , (Academic Press Limited), Third Edition, pp. 517-547 (1998).
C57	GenBank Accession No. AC010149, "Homo sapiens BAC clone RP11-395A23 from 2, complete sequence," (2005) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C58	GenBank Accession No. AF165167, "Homo sapiens high mobility group 1-like protein L8 (HMG1L8) retropseudogene, complete sequence," (2001) [online] [retrieved on 4/21/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C59	GenBank Accession No. AF076674, "Homo sapiens high mobility group 1-like protein L1 (HMG1L1) retropseudogene sequence," (1999) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C59	GenBank Accession No. AF076676, "Homo sapiens high mobility group 1-like protein L4 (HMG1L4) retropseudogene sequence," (1999) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C61	GenBank Accession No. NG_000897, "Homo sapiens high-mobility group (nonhistone chromosomal) protein 1-like 5 (HMG1L5) pseudogene on chromosome 3," (2006) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C62	GenBank Accession No. U51677, "Human non-histone chromatin protein HMG1 (HMG1) gene, complete cds," (1996) [online] [retrieved on 3/21/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C63	GenBank Accession No. XM_066789, "Homo sapiens similar to high mobility group 1 (LOC139603), mRNA," (2002) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>May 31, 2006</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. <b>3268.1003-004</b>  FIRST NAMED INVENTOR <b>Kevin J. Tracey</b>  EXAMINER <b>Not Assigned</b>	APPLICATION NO. <b>10/535,267</b>  FILING DATE <b>November 22, 2005</b>  CONFIRMATION NO. <b>6690</b> GROUP <b>1642</b>
---	--	---

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C64	GenBank Accession No. AF165168, "Homo sapiens high mobility group 1-like protein L9 (HMG1L9) retropseudogene complete sequence," (2001) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C66	GenBank Accession No. XM_063129, "Homo sapiens similar to high mobility group 1 (LOC122441), mRNA," (2002) [online] [retrieved on 4/18/2006]. Retrieved from the Internet: <URL:http://www.ncbi.nlm.nih.gov>.
C66	"High Mobility Group, (HMG) Chromosomal Proteins Nomenclature Home Page" [online] [retrieved on Mrach 9, 2006]. Retrieved from the Internet:<URL:http://www.informatics.jax.org/mgihome/nomen/genefamilies/hmgfamily.shtml>
C67	Reeves, R. and Nissen, M.S., "The A•T-DNA-binding Domain of Mammalian High Mobility Group I Chromosomal Proteins," <i>J. Biol. Chem.</i> , 265(15):8573-8582 (1990).
C68	Taguchi, A., <i>et al.</i> , "Blockade of RAGE-amphoterin Signalling Suppresses Tumour Growth and Metastases," <i>Nature</i> , 405:354-360 (2000).
C69	Taudte, S., <i>et al.</i> , "Interactions Between HMG Boxes," <i>Protein Eng.</i> , 14(12):1015-1023 (2001).
C70	SWISS-PROT Accession Number P09429, "High Mobility Group Protein 1 (HMG-1) (High Mobility Group Protein B1)," [online] [retrieved on 03/09/2006]. Retrieved from the Internet:<URL:http://www.ncbi.nlm.nih.gov>.
C71	Marks, J.D., <i>et al.</i> , "By-Passing Immunization: Building High Affinity Human Antibodies by Chain Shuffling," <i>Bio/Technology</i> , 10:779-783 (1992).
C72	Redlitz, A., <i>et al.</i> , "Receptors for Plasminogen and t-PA: An Update," <i>Bailliere's Clinical Hematology</i> , 8(2):313-327 (1995).
C73	Vassalli, J.-D., <i>et al.</i> , "The Plasminogen Activator/Plasmin System," <i>J. Clin. Invest.</i> , 88:1067-1072 (1991).
C74	Tomita, N., <i>et al.</i> , "Direct In Vivo Gene Introduction into Rat Kidney," <i>Bioch. Biophys. Res. Commun.</i> , 186(1):129-134 (1992).

EXAMINER	DATE CONSIDERED
----------	-----------------



PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>May 31, 2006</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3268.1003-004		APPLICATION NO. 10/535,267	
	FIRST NAMED INVENTOR Kevin J. Tracey		FILING DATE November 22, 2005	
	EXAMINER Not Assigned		CONFIRMATION NO. 6690	GROUP 1642

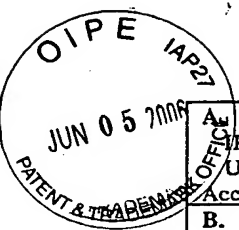
**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

C75	Jakobovits, A., <i>et al.</i> , "Analysis of Homozygous Mutant Chimeric Mice: Deletion of the Immunoglobulin Heavy-Chain Joining Region Blocks B-Cell Development and Antibody Production," <i>Proc. Natl. Acad. Sci. USA</i> , 90:2551-2555 (1993).
C76	Jakobovits, A., <i>et al.</i> , "Germ-Line Transmission and Expression of a Human-Derived Yeast Artificial Chromosome," <i>Nature</i> , 362:255-258 (1993).
C77	Ohlin, M., <i>et al.</i> , "Human Monoclonal Antibodies Against a Recombinant HIV Envelope Antigen Produced by Primary <i>in vitro</i> Immunization. Characterization and Epitope Mapping," <i>Immunology</i> , 68:325-331 (1989).
C78	Sjögren-Jansson, E., <i>et al.</i> , "Production of Human Monoclonal Antibodies in Dialysis Tubing," <i>Hybridoma</i> , 10(3):411-419 (1991).
C79	Pulkki, K., "Cytokines and Cardiomyocyte Death," <i>Ann. Med.</i> , 29:339-343 (1997).
C80	Tsutsui, H., <i>et al.</i> , "Pathophysiological Roles of Interleukin-18 in Inflammatory Liver Disease," <i>Immunol. Rev.</i> , 174:192-209 (2000).

EXAMINER	DATE CONSIDERED
----------	-----------------



# COPY



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36975

### A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 5/00, 16/00; A61K 39/395; C12N 15/00  
US CL : 530/350, 387.3, 388.8; 424/134.1, 155.1; 435/69.7

According to International Patent Classification (IPC) or to both national classification and IPC

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350, 387.3, 388.8; 424/134.1, 155.1; 435/69.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WEN et al. A Human Placental cDNA Clone that Encodes Nonhistone Chromosomal Protein HMG-1. Nucleic Acids Research. 1989, Vol. 17, No. 3, pages 1197-1213, see Figure 6.	1-5.
Y		7-9.
Y	LODE et al. Targeted Cytokines for Cancer Therapy. Immunologic Research. 2000, Vol. 21, No. 2-3, pages 279-288, see pages 280-281.	10-22, 24-26, 28-35, 37-39, 41-45.
Y	CZURA et al. Dual Roles for HMGB1: DNA Binding and Cytokine. Journal of Endotoxin Research. 2001, Vol. 7, No. 4, pages 315-321, see entire document, particularly Table 1 and pages 318-319.	10-22, 24-26, 28-35, 37-39, 41-45.
Y	ANDERSSON et al. High Mobility Group I Protein (HMG-1) Stimulates Proinflammatory Cytokine Synthesis in Human Monocytes. Journal of Experimental Medicine. August 2000, Vol. 192, No. 4, pages 565-570, see entire document, particularly page 569.	10-22, 24-26, 28-35, 37-39, 41-45.
Y	US 6,649,172 B2 (JOHNSON) 12 December 2001 (12.12.2001), see column 41.	7-9, 24-26, 37-39.



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;"

document member of the same patent family

Date of the actual completion of the international search

09 July 2004 (09.07.2004)

Date of mailing of the international search report

02 AUG 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703) 872-9306

Authorized officer

Valerie Bell-Harris for  
David J. Blanchard

Telephone No. (571) 272-1600



# INTERNATIONAL SEARCH REPORT

International application No.:

PCT/US03/36975

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.



**INTERNATIONAL SEARCH REPORT**

PCT/US03/36975

**Continuation of B. FIELDS SEARCHED Item 3:**

WEST, Medline, Biosis, cancerlit, biotechno, embase, caplus.

Search terms: HMGB or high mobility group box, HMG-1, immunostimulant, adjuvant, CpG, monophosphoryl lipid A, cancer or tumor, inventor search.